Epidemiologic Analyses of Risk Factors for Bone Loss and Recovery Related to Long-duration Space Flight

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Overview

- Study Overview
- Progress on Aims
- Unexpected Challenges

Response to NRA

- To address:
  - the risk of long-term effects on crew health regarding bone loss and fracture
  - the need to define the likelihood and/or consequence of bone health recovery post-flight

Study Overview

- Collaboration between NASA-JSC and Mayo Clinic, Rochester MN.
- Analyses of BMD and risk factor data already collected on US crew, with comparisons to a population-based cohort (Rochester Bone Health Study).

Specific Aims

AIM 1: To investigate the risk of microgravity exposure on long-term changes in bone health and fracture risk.

- compare data from crew members ("observed") with what would be "expected" from Rochester Bone Health Study.

AIM 2: To provide a summary of current evidence available on potential risk factors for bone loss, recovery & fracture following long-duration space flight.

- integrative review of all data pre, in-, and post-flight across disciplines (cardiovascular, nutrition, muscle, etc.) and their relation to bone loss and recovery

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Methods

- "Expected" BMD changes were determined based on data from the Rochester Bone Health Study cohort of 699 men and women, representing an age-stratified random sample of the adult community (age 20-95 years)
- "Observed" BMD changes following long-duration flight from 28 crew members were measured:
  - Immediately post-flight
  - ~1 year post-flight

Rochester Bone Health Study

- 348 men, age range at baseline: 22-90 years
- 351 women, age range at baseline: 21-93 years

- BMD measurements on Hologic QDR 2000 at spine, hip, radius, total body.

- BMD at baseline, 2 and 4 years for men.
- BMD at baseline, 1, 2 and 4 years for women.

Rochester Bone Health Study

- Prediction models derived using baseline and follow-up BMD data from cohort
- Prediction of “expected” BMD over follow-up using:
  - Linear mixed effects models
  - Baseline BMD, age at baseline BMD, gender, and time-to-follow-up, as predictors in model
  - Models including body mass index and total lean mass as predictors were also considered

Long-Duration Crew

- 28 men and women
  - 24 men, age range at preflight scan: 36-53 yrs
  - 4 women, age range at preflight scan: 41-53 yrs

- BMD measurements on Hologic QDR 2000, QDR 4500 and Discovery at spine, hip, radius, total body.

- BMD pre-flight, immediately post flight and ~1 year post-flight

Long-Duration Crew

- Median flight duration: 167 days (range: 95-215 days)
- Immediate post-flight BMD performed a median of 6 days (range: 3-33 days) following return on 24 men and 4 women.
- ~1 year post-flight BMD performed a median of 376 days (range: 184-534 days) following return on 22 men and 4 women.

Long-Duration Crew

- 25/28 had pre-flight BMD performed within 6 months before launch (all 28 had immediate post-flight BMD)
  - 24/25 had pre- and immediate post-flight BMD on same machine (7 QDR 2000, 11 QDR 4500 and 6 on Discovery)
- 24/28 have a pre-flight BMD within 6 months of flight and a post-flight BMD within 6-18 months of return. (26/28 had a 6-18 month BMD)
  - 22/24 have scans on same machine (7 QDR 2000, 10 QDR 4500 and 5 Discovery)

BMD Site*	Mean Pre-Flight BMD (g/cm^2) (Used first and last pre-flight scans available)		
	Expected	Observed	
	BMD	BMD	p-value
Total Hip	1.106	1.097	0.11
Lumbar Spine	1.091	1.080	0.04
Mid Shaft Radius	0.713	0.702	0.06
Ultradistal Radius	0.525	0.529	0.37
Total Body	1.284	1.281	0.75

N=25 for all sites except radius sites where N=17

BMD Site*	Mean Immediate Post-Flight BMD (g/cm^2) % Change per Month (% chg/mos)				
	Expected		Observed		
	BMD	% chg/mos (95% CI)	BMD	% chg/mos (95% CI)	p-value
Total Hip	1.082	-0.00 (-0.05, 0.04)	1.012	-0.87 (-1.04, -0.71)	<0.001
Lumbar Spine	1.078	0.12 (0.10, 0.13)	1.028	-0.48 (-0.61, -0.34)	<0.001
Mid Shaft Radius	0.710	0.17 (0.11, 0.23)	0.695	-0.06 (-0.17, 0.04)	0.001
Ultradistal Radius	0.519	-0.02 (-0.05,-0.00)	0.511	-0.21 (-0.34, -0.09)	0.01
Total Body	1.264	-0.05 (-0.05,-0.04)	1.240	-0.26 (-0.37, -0.16)	0.002

N=25 for all sites except radius sites where N=17

BMD Site*	Mean ~1 Year Post-Flight BMD (g/cm^2) % Change per Month (% chg/mos)				
	Expected		Observed		
	BMD	% chg/mos (95% CI)	BMD	% chg/mos (95% CI)	p-value
Total Hip	1.086	0.01 (-0.01, 0.02)	1.062	-0.10 (-0.15, -0.06)	<0.001
Lumbar Spine	1.086	0.05 (0.05, 0.06)	1.068	-0.03 (-0.01, 0.03)	0.004
Mid Shaft Radius	0.705	0.06 (0.03, 0.09)	0.694	-0.01 (-0.06, 0.04)	0.02
Ultradistal Radius	0.512	-0.07 (-0.07,-0.06)	0.517	-0.02 (-0.07, 0.02)	0.03
Total Body	1.264	-0.02 (-0.03,-0.02)	1.248	-0.08 (-0.15, -0.01)	0.08

**N=24 for all sites except radius sites where N=16*

Findings to Date

- Our simple BMD prediction models appear to work well…
- Models including body mass index or lean mass yielded similar findings, but work is ongoing to improve models.
- Overall, BMD ~1 year post-flight still show lower than expected BMD values at most sites, particularly weightbearing sites.
- Still exploring differences between men and women

Unexpected Challenges…

- Signed consent required to access and view collected data from long-duration crew as age, gender, race/ethnicity are attributable data.
- Inability to export data with scan dates or flight dates, despite informed consent.
- Recently informed that will also need signed consent to access short-duration crew BMD.

Lack of 100% consent limits access and analyses of available data which may have potential limitations on interpretation of results.

Other Unexpected Challenges…

- Took >1 year to achieve secure remote access from Mayo Clinic to JSC-NASA in order to view and export data.
- Lack of standardized procedures for data access
  - Establishment of standards with concurrent input from CPHS (Committee for the Protection of Human Subjects), LSAH (Longitudinal Study of Astronaut Health) and Crew Office would be ideal

On-going work

- Better calibration of BMD between 2 cohorts at each region of interest using pre-maiden flight BMD from all US crew members available.
- Assembly of risk factor data available from long-duration crew
- Further refinement of fracture prediction models based on Rochester cohort using BMD, risk factor data collected and observed fractures over ~20 years of follow-up.